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(See the editorial commentary by Austin, on pages 593–594.)

Background. Foodborne botulism resulting from consumption of uncooked aquatic game foods has been an endemic hazard among Alaska Native populations for centuries. Our review was conducted to help target botulism prevention and response activities.

Methods. Records of Alaska botulism investigations for the period 1947–2007 were reviewed. We used the Centers for Disease Control and Prevention case definitions for foodborne botulism and linear regression to evaluate incidence trends and $\chi^2$ or Fisher’s Exact tests to evaluate categorical data.

Results. A total of 317 patients (61% of whom were female) and 159 outbreaks were reported. Overall mean annual incidence was 6.9 cases per 100,000 Alaska Native persons; mean incidence was lower in 2000 (5.7 cases per 100,000 Alaska Native persons) than in any period since 1965–1969 (0.8 cases per 100,000 Alaska Native persons). Age-specific incidence was highest (26.6 cases per 100,000 Alaska Native persons) among persons aged ≥60 years. The overall case-fatality rate was 8.2%, and the case-fatality rate was ≤4.0% since 1980. Misdiagnosis was associated with a higher case-fatality rate and delayed antitoxin administration.

Conclusions. Foodborne botulism remains a public health problem in Alaska. Incidence might be decreasing, but it remains >800 times the overall US rate (0.0068 cases per 100,000 persons). Prevention messages should highlight the additional risk to female individuals and older persons. Early diagnosis is critical for timely access to antitoxin and supportive care.
surveillance and response remain major activities for the Alaska Division of Public Health (ADPH), which staffs a 24-hour botulism emergency consultation service.

We reviewed epidemiologic records to improve understanding of demographic and regional factors associated with botulism in Alaska and to guide ongoing ADPH botulism prevention efforts. Our findings should be useful to clinicians and public health professionals in other regions where foodborne botulism is encountered and to persons engaged in botulism research, response, and bioterrorism preparedness activities in areas where naturally occurring foodborne botulism is too rare to be adequately studied.

METHODS

Study Population and Traditional Alaska Native Foods

An Alaska Native person is a member of an indigenous population group in Alaska. Combined, these groups comprised 16% of the 2007 Alaska population of ~674,000 persons [11]. A traditional Alaska Native aquatic game food was a non-commercial food that was obtained from a fish, marine mammal (eg, whale, seal, and walrus), or beaver.

Data Sources

Epidemiologic records of foodborne botulism investigations during 1947–2007 were reviewed at the ADPH and the CDC Arctic Investigations Program in Anchorage, Alaska. Foodborne botulism is a public health emergency, and suspected cases are immediately investigated. For certain outbreaks during 1947–1962, epidemiologic investigations were conducted by the Indian Health Service, and laboratory tests were conducted at the University of British Columbia or the George Williams Hooper Foundation in San Francisco, California [2, 12–14]. All other investigations and laboratory testing were conducted by the ADPH or the CDC.

Case Definitions and Laboratory Confirmation

A probable case was defined as illness compatible with botulism in a person who had consumed a traditional Alaska Native aquatic game food [15]. A confirmed case was defined as a clinically compatible case that was laboratory-confirmed or occurred in a person who had eaten the same implicated food as a person with a laboratory-confirmed case.

A clinically compatible case of botulism included evidence of cranial nerve palsy (blurred vision, diplopia, dilated pupils, ptosis, dysphagia, dysarthria, or dysphonia) with or without other botulism signs or symptoms, including dry mouth, nausea, vomiting, abdominal pain, constipation, ileus, urinary retention, muscle weakness in the extremities, or respiratory muscle weakness [8, 16]. Botulism was defined as severe if death or signs or symptoms of respiratory muscle weakness were present. The case location was the village or city where illness onset occurred. An outbreak was any occurrence of foodborne botulism, whether a single case or a cluster of ≥2 cases (either probable or confirmed), that was associated with the same epidemiologically implicated food. Laboratory confirmation required detection of botulinum toxin in serum, gastric fluid, stool, or food or isolation of C. botulinum from stool or gastric fluid by standard methods [17].

Case Information and Statistical Methods

For each case, we recorded the clinical signs and symptoms, date of illness onset, initial clinical diagnosis and treatment, and whether the patient had survived the illness. We could not determine whether unrecorded clinical symptoms and signs were absent or were not sought. Analyses of factors associated with fatal botulism were restricted to the period 1970–2007, because access to respiratory supportive care was limited before 1970. The food source, preparation methods, and date of consumption of suspected foods were recorded. The incubation period was the time between consumption of the implicated food and illness onset [18].

Denominators reflect cases for which relevant data were available. Incidence was estimated with the median Alaska Native population from each period [11, 19]. Population counts for intercensal years were based on estimates. Annual stratifications of Alaska Native census data by sex and age group have been available since 1970. We used simple linear regression to evaluate incidence trends among demographic groups (weighted by group population) and changes in patient age across time. The χ² or Fisher’s exact tests were used to compare categorical variables, and the Mann-Whitney U test was used for continuous variables. Binary logistic regression was used to model predictors of fatal botulism including age, toxin type, and single cases (vs cluster-associated cases) [18, 20], as well as initial misdiagnosis of botulism. Model goodness-of-fit was evaluated with Hosmer and Lemeshow’s χ² test. Statistical tests were conducted at the .05 level of significance, except for subgroup comparisons among toxin types A, B, and E, which were conducted at the .017 level (Bonferroni correction). Analyses were performed with SPSS statistical software, version 17.0 (SPSS). Locations of botulism outbreaks were mapped with ArcGIS software, version 9.3 (ESRI). This review of routinely collected surveillance records was determined not to be human subjects research by a CDC human subjects contact.

RESULTS

Epidemiology of Cases

Cases and Deaths. During the period 1947–2007, 317 cases of foodborne botulism were reported, including 258 (81%) confirmed and 59 (19%) probable cases. All patients were identified as Alaska Native. The mean annual number of cases was 5.2 (range, 0–31 cases per year). Three persons had experienced
repeated illnesses of botulism. The mean annual incidence was 6.9 cases per 100,000 Alaska Native persons overall and was lower during 2000–2004 (5.6 cases per 100,000 Alaska Native persons) and 2005–2007 (5.9 cases per 100,000 Alaska Native persons) than during any other period since the all-time low incidence during the period 1965–1969 (0.8 cases per 100,000 Alaska Native persons) (Figure 1). The case-fatality rate was 8.2% (26 deaths among 317 patients) overall and decreased (P < .001) from 57.1% during 1947–1949 to <4.0% during each period after 1970–1979 (Figure 2).

Incidence by Sex and Age. Sixty-one percent (191 of 311) of the patients were female. During 1970–2007, the mean annual incidence per 100,000 Alaska Natives was 11.4 cases for female individuals and 6.5 cases for male individuals (Figure 1). Overall median age was 45.0 years (range, 5–93 years). Incidence was associated with age group (P < .001); age group–specific incidence was greatest among Alaska Natives aged ≥60 years (26.6 cases per 100,000 Alaska Native individuals) (Figure 3a). The relation between incidence and age group remained when stratified by period (P < .001 for each period) (Figure 3b). Patient age increased from 1970–1979 (median age, 39.0 years) to 2000–2007 (median age, 49.5 years; P < .001).

Incubation Period. Incubation period could be estimated in days for 82% (259 of 317) of the patients and in hours for 41% (130 of 317) of the patients. Median incubation period was within 1 day (16 h), and the range was 0–7 days (1–84 h); 90% of the patients experienced onset within 2 days (30 h). Incubation periods were similar among toxin types.

Epidemiology of Outbreaks

Number, Size, and Seasonality. A total of 159 foodborne botulism outbreaks were reported, including 87 single cases and 72 multiple-case outbreaks. The mean number of cases per outbreak was 2.0 (range, 1–9 cases), and 90% of outbreaks involved ≤3 cases. Seasonality was observed; 78% (124 of 159) of the outbreaks occurred during May–October, with 38% (61 of 159) occurring during July–August alone. Only 6% (10 of 159)
of the outbreaks were reported from cities with populations >10,000 persons as reported in the year 2000 (5 outbreaks each in Anchorage and Juneau, which together accounted for 20% of the Alaska Native population) [19].

### Frequency and Geographic Distribution of Outbreaks by Toxin Type

Of 129 outbreaks in which a toxin type was reported, 107 (83%) were caused by type E, 17 (13%) by type B, 4 (3%) by type A, and 1 (1%) by mixed types B and E that...
was confirmed by isolation of *C. botulinum* types B and E from gastric fluid. Type E botulism occurred in all areas in which botulism was reported, and type A outbreaks were uncommon (Figure 4). Among 18 outbreaks that involved type B botulism, 94% (17 outbreaks) were clustered in southwestern Alaska (Figure 4). The 1 other type B outbreak occurred in Anchorage and involved seal blubber shipped from western Alaska.

**Implicated Foods.** Among 141 outbreaks in which a single food was implicated, all foods were of aquatic animal origin, including fish (48%), marine mammals (47%), and beaver (6%) (Table 1). Salmon eggs were associated with 95% (20 of 21) of the outbreaks in southeastern Alaska, 95% (63 of 66) of the outbreaks associated with marine mammals occurred in southwestern or northern Alaska, and 100% (8 of 8) of the outbreaks involving beaver occurred in the Bristol Bay area (Table 1). In regions with multiple toxin types, foods did not differ according to toxin type.

Among outbreaks with available information regarding food preparation, 95% (125 of 131 outbreaks) involved uncooked, home preserved aquatic game foods; 2% (3 of 131) involved skin and blubber that had been consumed directly from a decomposing whale or seal carcass; 2% (2 of 131) involved dried fish (including 1 outbreak in which the dried fish had appeared spoiled); and 1% (1) involved fish soup that had been eaten immediately after boiling for >1 h and again the next day after being stored on a table next to a woodstove. Regardless of preparation method, 7% (9 of 131) of the outbreaks involved foods that had been collected from decomposing whale or seal carcasses found on beaches or floating at sea.

Among outbreaks for which a preservation process was described, 67% (56 of 84) were associated with storage of food in sealed plastic or glass containers, 23% (19 of 84) with storage in wood or cardboard containers, 6% (5/84) with storage in sealed metal containers, 4% (3/84) with storage in moss- or tundra-covered holes, and 1% (1/84) with storage in a sealskin bag.

**Clinical Care, Diagnosis, and Case-fatality**

**Hospitalization and Treatment.** The percentage of patients hospitalized during 1947–1970 (88%) was similar to the percentage of patients hospitalized during 1970–2007 (87%). Before 1970, antitoxin E was unavailable; 8% (2 of 24) of the patients had received bivalent antitoxin AB, and 15% (3 of 20) had received ventilatory support. During the period 1970–2007, 76% (199 of 263) of the botulism patients had received antitoxin types A, B, and E, and 31% (74 of 235) had received mechanical ventilatory support. Since 1970, antitoxin has been administered to 95% (70 of 74) of the patients experiencing severe botulism versus 69% (128 of 185) experiencing non-severe botulism (*P* < .001). Data regarding underlying medical conditions, adverse reactions to antitoxin, overall duration of illness, and other sequelae were unavailable.

**Initial Diagnosis of Illness in Patients.** Botulism was suspected at the initial clinical presentation for 78% (159 of 203) of the cases. Initial misdiagnosis occurred in 28% of single cases and 18% of cases in multiple-case outbreaks (*P* = .124). When botulism was not suspected, the initial diagnosis was frequently a gastrointestinal or respiratory illness (Table 2). Among 155 patients for whom data were available, antitoxin was administered a median of 1 day (mean, 1.78 days) after illness onset when botulism was initially suspected and a median of 3 days (mean, 3.51 days) when botulism was initially misdiagnosed (*P* < .001).

**Factors Associated with Fatal Botulism, 1970–2007.** Fatal botulism (*n = 14*) was more prevalent among single cases and cases associated with patient age ≥45 years, initial misdiagnosis, and type A botulism (Table 3); case fatality rates did not differ among patients with types B and E botulism (*P* = .157). The 6 fatal cases that involved initial misdiagnosis included 4 cases in patients who had not received antitoxin or mechanical

<table>
<thead>
<tr>
<th>Aquatic game food source</th>
<th>Total, % (n=141)</th>
<th>Southeast (n=21)</th>
<th>Central (n=7)</th>
<th>Southwest (n=75)</th>
<th>Northern (n=38)</th>
<th>Most recent year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish, any</td>
<td>47.5</td>
<td>100.0</td>
<td>57.1</td>
<td>50.7</td>
<td>10.5</td>
<td>2007</td>
</tr>
<tr>
<td>Fish eggs</td>
<td>18.4</td>
<td>95.2</td>
<td>28.6</td>
<td>2.7</td>
<td>5.3</td>
<td>2006</td>
</tr>
<tr>
<td>Fish heads</td>
<td>14.9</td>
<td>4.8</td>
<td>28.6</td>
<td>22.7</td>
<td>2.6</td>
<td>2007</td>
</tr>
<tr>
<td>Fish, other</td>
<td>14.2</td>
<td>...</td>
<td>...</td>
<td>25.3</td>
<td>2.6</td>
<td>2007</td>
</tr>
<tr>
<td>Seal, any</td>
<td>31.2</td>
<td>28.6</td>
<td>29.3</td>
<td>52.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seal oil or blubber</td>
<td>22.7</td>
<td>...</td>
<td>28.6</td>
<td>24.0</td>
<td>31.6</td>
<td>2007</td>
</tr>
<tr>
<td>Seal flipper</td>
<td>7.8</td>
<td>...</td>
<td>...</td>
<td>4.0</td>
<td>21.1</td>
<td>1999</td>
</tr>
<tr>
<td>Seal meat</td>
<td>0.7</td>
<td>...</td>
<td>...</td>
<td>1.3</td>
<td>...</td>
<td>1988</td>
</tr>
<tr>
<td>Whale fluke, skin or blubber</td>
<td>13.5</td>
<td>...</td>
<td>8.0</td>
<td>34.2</td>
<td></td>
<td>2007</td>
</tr>
<tr>
<td>Beaver tail or paw</td>
<td>5.7</td>
<td>...</td>
<td>10.7</td>
<td>...</td>
<td></td>
<td>2007</td>
</tr>
<tr>
<td>Walrus oil, blubber, or flipper</td>
<td>2.1</td>
<td>...</td>
<td>14.3</td>
<td>1.3</td>
<td>2.6</td>
<td>1989</td>
</tr>
</tbody>
</table>

**Note.** Data are for 141 outbreaks in which a specific food source was identified.
ventilation. In a binary logistic regression model ($\chi^2 = 2.126; P = .908$), misdiagnosis and toxin type were significant predictors of fatal botulism (Table 3).

## Conclusions

Foodborne botulism remains a potentially fatal public health risk among Alaska Native persons. Incidence decreased between 1985–1989 and 2000–2004 and remained lower during 2000–2007 than during any period since the 1960s. The recent decrease illustrates the impact of statewide prevention efforts [7–9]. Improved surveillance and clinical recognition of cases might have contributed to the increase after the 1960s, although reports from the 1970s indicate that the increase was perceived as real and attributed to changing food preservation practices [5, 21]. However, mean annual incidence among Alaska Natives during the period 2000–2007 was 836 times the overall US rate of foodborne botulism (0.0068 cases per 100,000 persons; CDC surveillance data, March 2010) [19].

Across time, botulism incidence among Alaska Native persons remained higher among the female population and older age groups, and occurrence of outbreaks peaked during late summer. Food consumption practices were not assessed in our study. Previous surveys have reported more frequent consumption of uncooked aquatic game foods among the female population and older Alaska Native persons than among the male population or younger persons [6, 9]. The seasonality of botulism outbreaks has been described previously [8] and is probably related to warmer temperatures and seasonal dietary variations. Educational materials related to botulism prevention should be disseminated to rural Alaska Native communities each spring, with messaging that targets the female population and older persons.

Similar patterns of foodborne botulism have been described among Canadian and other circumpolar indigenous populations [2, 22]. For example, salmon eggs are the principal etiology of botulism in both southeastern Alaska and neighboring British Columbia, and marine mammal foods have been more frequently associated with botulism in northern regions of both Alaska and Canada. International partnerships for the

### Table 3. Characteristics of Fatal Botulism Cases ($n = 14$) among Alaska Native Persons, Alaska, 1970–2007

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nonfatal illness, %</th>
<th>Fatal illness, % ($n = 14$)</th>
<th>Unadjusted $P$</th>
<th>$P$, binary logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age category, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5–44 ($n = 139$)</td>
<td>97.8</td>
<td>2.2</td>
<td>.032$^a$</td>
<td>.085</td>
</tr>
<tr>
<td>45–93 ($n = 142$)</td>
<td>92.3</td>
<td>7.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single case ($n = 80$)</td>
<td>91.3</td>
<td>8.8</td>
<td>.070$^b$</td>
<td>.207</td>
</tr>
<tr>
<td>Multicase outbreak ($n = 207$)</td>
<td>96.6</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxin type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A ($n = 9$)</td>
<td>66.7</td>
<td>33.3</td>
<td>&lt;.001$^a$</td>
<td>.025</td>
</tr>
<tr>
<td>B ($n = 41$)</td>
<td>100.0</td>
<td>...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E ($n = 191$)</td>
<td>95.3</td>
<td>4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Misdiagnosed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No ($n = 144$)</td>
<td>97.2</td>
<td>2.8</td>
<td>.012$^b$</td>
<td>.007</td>
</tr>
<tr>
<td>Yes ($n = 44$)</td>
<td>86.4</td>
<td>13.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** Restricted to 1970 or thereafter because antitoxin and respiratory supportive care were limited before 1970.

$^a$ Pearson’s $\chi^2$.

$^b$ Fisher exact test.
development of effective prevention strategies should be considered.

The historical decrease in case-fatality rates corresponded to improved access to effective antitoxin and mechanical ventilation. This decrease could have been overestimated if statewide education campaigns led to greater recognition and reporting of milder botulism. Fatal botulism was associated with initial misdiagnosis with or without adjustment for factors that have been previously associated with severe and fatal botulism, including age, toxin type, and case status (single cases or mult case outbreaks) [18, 20]. Misdiagnosis was associated with a median 2-day delay in antitoxin administration and was a factor in 4 fatal cases that occurred before antitoxin or mechanical ventilatory support was provided. Although our database is among the largest yet evaluated, we did not evaluate the benefit of antitoxin for outcomes because severity at presentation was the primary determinant of antitoxin receipt, and almost all patients who experienced severe symptoms had received antitoxin. Clinical follow-up data were not systematically recorded in the epidemiologic records, and clinical reviews of hospitalized Alaska botulism patients are available from earlier periods [21, 23].

Botulism antitoxins are considered most effective when administered within the first 24–48 h of illness [18, 20], although circulating botulinum neurotoxin has been detected up to 11 days after symptom onset among Alaska Native patients [24]. In Alaska villages, access to regional hub hospitals with antitoxin and mechanical ventilators usually requires transportation by aircraft. Thus, early recognition of botulism is critical to ensure timely access to antitoxin and mechanical ventilatory support [21]. Eliciting a history of consumption of uncooked aquatic game foods can aid in the correct diagnosis of botulism, including among patients who initially present with nonspecific gastrointestinal or respiratory syndromes. The ADPH should continue to maintain and disseminate a botulism guide to physicians and village health aides statewide [8].

Nontraditional food-storage containers were implicated when Alaska botulism incidence increased during the 1970s and 1980s [5, 6, 9]. In a 2001 survey, one-third of Alaska Native food preparers who stored uncooked aquatic game foods did so with synthetic plastic or metal containers [10]. In this review, two-thirds of botulism outbreaks were associated with preservation of foods in sealed plastic or glass containers. Anaerobic conditions and warmer temperatures associated with above-ground food preservation in sealed containers provide favorable conditions for toxin elaboration by *C. botulinum* [6, 7, 25]. Still, traditional preservation methods alone will not eliminate the risk for botulism associated with consumption of uncooked aquatic game foods. First, botulism was associated with these foods before synthetic containers became available to Alaska Native and other northern indigenous populations [1, 2, 13]. Second, outbreaks involving foods eaten directly from dead marine mammals continue to occur [26]. Nontraditional food preservation methods should be discouraged, but educational messages should also highlight the risk for consuming unpreserved food from dead aquatic game animals and promote adequate cooking of aquatic game foods as the most effective means to eliminate risk for botulism.

*C. botulinum* type E has been isolated from aquatic sediments and animals in Alaska [27–31]. An environmental source has not been identified for *C. botulinum* type B, and past investigations have usually not included the region where approximately all type B botulism outbreaks occur in Alaska. Epidemiologic data indicate that the environmental sources of *C. botulinum* type B might be located inland along the Kuskokwim River drainage and contiguous area to the south; additional environmental investigation might identify where in the aquatic game food collection and preservation process contamination with *C. botulinum* likely occurs.

In March 2010, bivalent botulism antitoxin AB and monovalent antitoxin E were replaced nationwide with investigational heptavalent botulinum antitoxin (HBAT) [32]. HBAT contains antitoxin against all known toxin types (ie, types A, B, C, D, E, F, and G) and eliminates the need to administer 2 separate antitoxin products to Alaskan patients. Experience in Alaska will provide critical information regarding use of HBAT for patients with foodborne botulism; indeed, the first US patient to receive this product for suspected foodborne botulism was an Alaska Native patient (L. J. Castrodale, personal communication).

Improved methods to reduce the risk for foodborne botulism and support behavior change should be explored. For example, an educational botulism video was distributed to all rural schools and medical facilities in Alaska, but 1 year after distribution, only 38% of Alaska Native adults had seen the video, and no behavior changes were noted that might reduce risk for botulism [10]. Other areas of potential future investigation include broader assessment of Alaska Native food preparation and consumption practices and description of long-term clinical sequelae from type E botulism.

**Acknowledgments**

We thank Duane Fridley, Alaska Department of Health and Social Services, for assistance with access to Alaska census data; and Amy Krueger, Centers for Disease Control and Prevention, for creation of the map. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

**Potential conflicts of interest.** B.G. is employed by AMP (Paris, France), which receives unrestricted and grant support from Aventis Pasteur, a manufacturer of botulism anti-toxin. All other authors: no conflicts.

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